(2)

DTIC FILE COPY

AD-A211 885

THE EFFECTS OF ADAPTATION TO A LOW CARBOHYDRATE/ HIGH FAT DIET AND PRE-EXERCISE FEEDING ON EXERCISE ENDURANCE, METABOLISM, AND CARDIOVASCULAR DYNAMICS IN SWINE

DTIC
ELECTE
SEP 0 5 1989
S D

CHARLES G. GRAY

20030203115

REPORT NO. 88-3

Approved for public release, distribution unlimited

NAVAL HEALTH RESEARCH CENTER
P.O. BOX 85122
SAN DIEGO, CALIFORNIA 92138

NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND
BETHESDA, MARYLAND

89 9 01133

THE EFFECTS OF ADAPTATION TO A LOW CARBOHYDRATE/HIGH FAT DIET AND PRE-EXERCISE FEEDING ON EXERCISE ENDURANCE, METABOLISM, AND CARDIOVASCULAR DYNAMICS IN SWINE

Charles G. Gray [a]
M. Dan McKirnan [b]
Francis C. White [b]
Larry Mandarino [b]
Grace Sun [c]
John Miles [d]

[a] Naval Health Research Center, P.O. Box 85122, San Diego, CA 92138-9174
[b] University of California San Diego, La Jolla, CA 92093
[c] University of Missouri, Columbia, MO 65211
[d] Mayo Clinic, Rochester, MN 55905

Report No. 88-3, supported by the U. S. Army Research Institute of Environmental Medicine, Nutrition Task Force under Work Unit No. 141. The views presented in this paper are those of the author(s) and do not reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U. S. Government.

Accession For
NTIS CRA&I
DTIC TAB
Unannounced
Justification
By
Distribution/
Availability Codes
Dist | Avail and/or Special
A-1

Summary

Field combat personnel may be required to sustain moderate intensity work loads for extended periods, while having to eat-on-the-run. The use of of a low carbohydrate (7% of calories)/high fat (74% of calories) diet (LCD) has been suggested as a means of improving endurance during moderate intensity exercise. Little is known about the interactions between preexercise eating and its effects on mechanisms of cardiovascular and metabolic control. A series of experiments were performed to establish a basis for manipulation of the metabolic system to improve exercise performance. Six groups of sedentary and exercise trained miniature swine were utilized to determine the effects of preexercise feeding and adaptation to a LCD on metabolism, moderate intensity exercise endurance, and cardiovascular dynamics. Data analysis has revealed important relationships between metabolic and cardiovascular control mechanisms. LCD adapted pigs ran an average 58 minutes longer than Control pigs when exercised at 65% of their heart rate reserve (moderate intensity exercise) and for up to 5 hours during tests. LCD pigs had higher blood glucose and lover blood lactate values than Control pigs at rest and during the runs to exhaustion. These data suggest a decreased utilization of carbohydrate as a fuel at rest and during exercise. Long term LCD adaptation (5 to 14 months) resulted in no increases in either blood triglycerides or cholesterol and no health or growth problems, suggesting no deleterious health effects. LCD adaptation also produced a decrease in insulin sensitivity indicating a possible application in treatment of hypoglycemic syndrome. Preexercise feeding resulted in reduced skeletal and cardiac muscle blood flows at identical exercise intensities in spite of an increased cardiac output needed for the digestive process. The finding of reduced myocardial blood flow, accompanying the increased blood flow demands for the digestive processes during exercise has implications related to the occurence of postprandial angina in man. The interactions between adaptation to a LCD and preexercise eating have potential application to enhancing performance of combat personnel. The interrelationships among these and other variables are briefly discussed.

Introduction

Field combat and special warfare personnel may be required to sustain moderate intensity work loads for extended durations with only brief rest periods interposed. Troops must also frequently eat-on-the-run during these extended operations. The preponderance of experimental work performed with regard to nutritional enhancement of exercise endurance has been performed at exercise intensities much higher than those sustained by combat personnel(6, 40). Existing data indicate that enhancement of exercise endurance can be most effectively achieved by preexercise augmentation of glycogen stores and carbohydrate (CHO) feeding during exercise. Currently available information on the interactions between exercise and preexercise eating on endurance, metabolism, and cardiovascular dynamics is very incomplete.

Long duration low intensity exercise at ~30% of maximal oxygen consumption (VO_2 Max)], produces a natural shift to the utilization of fat as the primary substrate (~90% of total energy) for muscle metabolism (2, 41). Improved endurance has resulted from both the acute elevation of plasma free fatty acids in rats (19) and the adaptation of humans (29, 30) and rats (26) to low CHO (1% of calories)/high fat (78-85% of calories) diets (LCD) for four to five weeks. The improvements were achieved by increasing the rate of fat utilization, while greatly reducing the rate of glucose and glycogen utilization. It was suggested that use of the LCD could improve endurance by athletes participating in prolonged endurance exercise over two or more days (29). Additionally, several studies have shown that intermittent exercise in normal diet individuals results in transient elevations of glucose and insulin during rest periods(9). Elevated insulin produces deleterious effects on fat metabolism by suppressing fat mobilization and accelerating glucose and glycogen utilization (1, 21), while inhibiting gluconeogenesis in the liver (1). The transient elevations in insulin during rest periods in normal diet individuals may necessitate periodic consumption of adequate amounts of CHO to keep pace with muscular requirements. Additionally, exercise has produced hypoglycemia (5, 31) which has resulted in decrements of psychomotor performance in some individuals (5). Elevated insulin during exercise may also cause wide swings in blood glucose concentration (1, 21) and, secondarily, could result in compromised cognitive function. Current

knovledge related to LCD and its applications is incomplete. Additional information on the mechanisms of metabolic regulation and adaptation is needed to efficiently utilize a LCD regime.

Potential advantages of utilizing the LCD for selected situations include decreased ration weight (higher caloric density), "greater efficiency of caloric utilization" (29), decreased dependency on frequency of eating, increased physical endurance, and increased cognitive performance as a result of reduced fluctuations in blood glucose during exercise. Due to lower biochemical transformation requirements for fat than glucose, a higher portion of fat calories eaten can be converted into work.

The effects on metabolism and evaluation of potential biochemical markers of LCD adaptation was measured by feeding the LCD to untrained pigs. The maximal adaptive response and potential deleterious effects on health were evaluated by feeding untrained pigs the LCD chow for more than a year. The combined effects of preexercise feeding and LCD adaptation were investigated by feeding the Control and LCD exercise trained pigs a meal of their accustomed diet just prior to prolonged moderate intensity exercise (65% VO_2 Max) on a motor driven treadmill. Control diet exercise trained pigs were studied following both fasting and feeding to determine the effects of feeding on cardiovascular dynamics, regional blood flow distribution, thermal regulation, and metabolism during long duration exercise. This report will summarize all of the results currently completed (some biochemical data incomplete), preliminary statistical analyses, brief comments on potential significance of the findings, and a very abbreviated reference list. Previous publications and presentations on these data are listed in the bibliography (10-16, 23-25).

Purposes

There were several purposes to the studies performed:

1. To measure the effects of chronic adaptation to a low carbohydrate/high fat diet (LCD) on endurance during moderate intensity exercise (MODX).
2. To determine the alterations in selected muscle and liver enzymes and blood concentrations and dynamic responses of glucose, lactate, lipids, insulin, and ketone bodies associated with short and long-term adaptations to the LCD.
3. To evaluate the effects of pre-exercise feedings on metabolism, thermoregulation, hemodynamics, regional blood flow distribution and endurance during MODX.
4. To measure the effects of diet and feeding on gastrointestinal metabolites and hormones during prolonged MODX.
5. To determine the metabolic, thermoregulatory and cardiovascular factors associated with exhaustion during prolonged MODX.

Methods

General Design. Six groups of miniature swine (total N=47) were studied. Blood samples were obtained at rest and during exercise either for metabolic measurements from the inferior vena cava (IVC) and the hepatic portal vein (PV) or for cardiovascular measurements (CV) from the pulmonary artery and descending aorta with the ability to inject substances into the left atrium. Two pigs were initially instrumented for IVC and PV sampling and later had catheters inserted through the carotid artery and internal jugular through the neck and into the ascending aorta and pulmonary artery, respectively. These two pigs were thus subjects for both metabolic and CV studies. Pigs in all groups except those used for CV studies had intercostal muscle, diaphragm muscle, and liver tissue samples taken during surgical catheter implantation procedures. The CV studies included cardiovascular dynamics (CVD) and regional blood flow distribution (RBF). Additional tissue samples were obtained at necropsy. Tissue samples were later analyzed for specific metabolic enzymes (EZ) as listed below.

Two untrained groups (N=19) were fed either the control diet (control untrained - CU) or the low carbohydrate/high fat diet (LCD untrained - DU). These animals underwent laparotomies, tissue biopsy procedures and standard intravenous glucose tolerance tests (GTT). A group of five untrained pigs received long-term feeding of the LCD (LTDU). The LTDU animals were fed the LCD from age 2 to 14-17 months. Tissue biopsies and GTTs were performed on the LTDU pigs. Two groups were endurance exercise trained and fed either the control diet (CT) or the LCD (DT). The 23 pigs in these two exercise groups underwent exercise training, laparotomies, tissue biopsy procedures, re-training, GTTs, meal feeding tests (MFT), maximal exercise tests (MXT) and runs to exhaustion (RTE). The final group of nine, control diet, trained pigs (CHT) were studied during two prolonged two-hour runs (R2HR) that followed either an overnight fast or a normal meal. Seven of these animals underwent thoracotomies prior to the runs, while two pigs were original members of the DT group and received additional catheters via a neck surgery. The groups' surgical procedures and tests performed are summarized in Table 1. Some animals were not tested due to illness.

Table 1. Animal Subject Groups and Procedures Performed

GROUP	No.	DIET	EXERCISE	SURGERY	TESTS
CONT Untrained	7	Control	NO	LAPAROTOMY	GTT, EZ
LCD Untrained	12	LCD	NO	LAPAROTOMY	GTT, EZ
CONT Trained	13	Control	YES	LAPAROTOMY	GTT, EZ, MFT, MXT, RTE
LCD Trained	10	LCD	YES	LAPAROTOMY	GTT, EZ, MFT, MXT, RTE
Long Term LCD Untrained	5	LCD	NO	LAPAROTOMY	GTT, EZ, MFT
CONT Trained (Microspheres)	9[a]	Control	YES	THORACOTOMY	MXT, R2HR, CVD, RBF

[a] The 9 Pigs in the CHT group include 2 pigs that had previously completed the DT testing procedures.

Experimental Diets. The composition of the experimental diets are listed in Table 2. Animals were gradually adapted from normal pig chow to these diets over a one week period. This involved a gradual change in proportions of pig chow and the experimental diet given in the twice daily feedings. This diet transition corresponded to the first week of habituation for trained animals, which permitted a 7 to 10 day period for diet adaptation prior to the start of training. Animals were fed twice daily totaling 4% of their body weight. Food not eaten was weighed back to determine daily caloric intake. Generally, weight back amounts were small unless the animal was sick or it was early in diet adaptation.

Table 2. Constituents of Synthetic Diets

	Control	Low Carbohydrate
Percent of total calories in chow mix:		
Carbohydrate	74	7
Fat	7	74
Protein	19	19
Percent by weight of constituents in chow mix:		
Meat & Bone Meal	8.5	13.5
Soybean Meal	28.5	23.0
Premix	.6	.5
Corn Oil	3.0	15.5
Tallow	0	15.5
Salt	.3	.3
Corn Starch	49.1	0
Dextrose	10.0	0
Vermiculite	0	12.5
Rice Hulls	0	19.2
Percent by weight of these nutrients:		
Calcium	.9	1.4
Phosphorus	.5	.8
Lysine	1.1	1.1
Methionine & Cystine	.5	.5

Exercise Training Protocol. Animals were familiarized to treadmill exercise for two weeks prior to initiation of exercise training. Treadmill familiarization progressed from low speed walking to slow running for 10 minute periods on three alternate days per week (MWF). Two maximal exercise tests (MXT) were used to establish the pre-training exercise capacity and maximal heart rate (HR) response. Training intensity was set at 65% of the maximum HR reserve [HR_{rest} +.65 (HR_{max} - HR_{rest})]. Animals were trained five days per week starting with 20 min/day for week one and progressed to 60 min/day by week six. Thereafter, animals trained 60 min/day, three to four days per week with a 30 min exercise bout on Wednesday. The appropriate training intensity was maintained by weekly heart rate monitoring and adjustment of the treadmill workload to correct for training adaptations. Prior to surgery, duplicate MXTs were conducted on separate days to ascertain the effects of training. Post-surgery animals were permitted to recover four to five days before initiating a re-training protocol. Re-training began with 10 minutes of slow walking and progressed to 30 minutes of regular training after week one. The 60 minute duration was achieved by the end of two weeks and continued into week three. MXTs were repeated at the end of week three to ascertain the state of training. Exercise experiments were initiated in the fourth week following surgery. Training adaptations were maintained during the period of experimentation by two to three days of training for 60 min/day at the prescribed intensity.

Maximal Exercise Testing (MXT). Animals were administered MXTs on a treadmill prior to training, following 8 weeks of training and prior to surgery, and after completing the three week recovery and re-training protocol. The test protocol was designed to elicit a maximal exercise response in approximately 12-15 minutes. The first three stages of 1.9 mph/5% grade, 3.1/5%, and 4.3/5% lasted three minutes and were consistent for all tests performed. This permitted an evaluation of submaximal adaptations to exercise training. Subsequently, the treadmill grade was increased by 2.5 or 5% every two minutes until the maximal work load had been achieved. The criteria for determining a maximal response were a plateau in heart rate despite an increase in external workload and/or fatigue as evidenced by an inability of the animal to maintain the work load despite repeated negative reinforcement. The maximal work load was then expressed in watts by the formula: speed(m/min) x (1+(% grade/100)) x

body weight(kg) divided by 6.12 (6.12 kg-m/min=1 watt). The maximal exercise tests provided determinations of both submaximal and maximal exercise responses.

Surgical Procedures. The concentration of substances in the blood draining the gastrointestinal tract and pancreas (GI) may undergo considerable alteration with passage through the liver. Therefore, it was necessary to measure blood samples from both the PV and IVC simultaneously. IVC and PV sampling enabled the comparison of blood concentrations of insulin, glucose, lactate, and blood gases in the two locations. Catheter placement for these measurements was accomplished via a laparotomy. These measurements allowed an assessment of the status of GI and liver function during the conditions of our testing. These measurements were desired to illustrate the participation of the GI system in the control of exercise metabolism. Measurement of cardiovascular dynamics (CVD) required implantation of indwelling catheters into the pulmonary artery, left atrium, and descending aorta via a thoracotomy. Fick techniques were used to measure cardiac output and gas exchange. Regional blood flow distribution (RBF) was measured by standard radiolabelled microsphere techniques (18). Oxygen consumption and carbon dioxide production were calculated by arterio-venous gas tension differences multiplied by the measured cardiac output.

Anesthesia was induced with ketamine (25 mg/kg) plus atropine (1/60 g) injected IM followed by sodium thiamylal (20 mg/kg) IV and maintained after intubation with halothane and oxygen. Skin regions around the incision and exit sites were shaved and scrubbed with provoiodine soap solution. Additionally, provoiodine solution was sprayed on the surgical sites prior to sterile draping. Exit sites for catheters were located adjacent to the spine in the intercostal spaces. The techniques for implanting the Gore-Tex$_{tm}$ peritoneal catheter at the skin interface have been extensively described elsewhere (13, 14).

Cannulation of the PV and IVC were performed with the animal lying on its left side via an oblique abdominal incision (laparotomy) just below the right costal margin at the level of the 12th to 15th rib and extended dorsally just superior to the right kidney. The intestines were retracted and catheters

were introduced through the intercostal exit sites adjacent to the dorsal spine. Two silastic catheters were introduced into the IVC and one in the PV. For all exercising pigs a silastic temperature port was introduced into the abdominal cavity and anchored near the kidney. The temperature port was a modified Gore-Tex$_{tm}$ interface with a sealed end within the abdominal cavity that permitted insertion of a thermistor probe from the exterior. The abdomen was closed in layers with 2-0 Vicryl (polyglactin) suture. Subcuticular 3-0 Vicryl was used to close the skin incisions on the abdomen and at the exit sites. Catheters were flushed with 1000 unit/ml heparin and sealed with rubber tipped intermittent infusion plugs (Argyle).

Cannulation of the great vessels of the heart was accomplished via a left lateral thoracotomy in the fourth intercostal space. Ribs and lungs were retracted for access to the left heart and aorta. Silastic catheters were introduced through the chest wall from exit sites adjacent to the dorsal spine. Two catheters were placed in the descending aorta. A small incision was made in the pericardium and catheters introduced into the pulmonary artery and left atrium. The pericardium was then closed with 3-0 Ethibond (Polybutilate coated Polyester) suture. The chest was closed in layers with 2-0 Vicryl. The skin incisions were closed with subcuticular 3-0 Vicryl. Catheters were flushed with saline and then retained with 1000 units/ml heparin and closed with a silk tie. The sealed catheters were then tucked into a subcutaneous pouch and the skin closed with subcutaneous 3-0 Vicryl. Following three weeks of recovery and re-training the catheters were exteriorized under general anesthesia. This technique of burying catheters subcutaneously at surgery has proven successful in preventing sinus tract infections and the resulting septicemia.

Catheterization of the ascending aorta and pulmonary artery (Swan-Ganz$_{tm}$) was accomplished by threading catheters into the left internal carotid and internal jugular, respectively. The catheters were exteriorized at exit sites on the dorsal neck. The incisions were closed with 2-0 and 3-0 Vicryl. Catheters were flushed with 1000 unit/ml heparin and sealed. The external catheters were coiled and secured on the dorsal neck with an elastic bandage.

Tissue biopsies using open biopsy techniques provided 100-200 mg samples of skeletal muscle and liver at the times of surgery and sacrifice. These samples were taken from CU, DU, CT, DT, and LTDU as required by the study design. The laparotomy permitted easy access to samples of the liver, diaphragm, and intercostal muscle. Liver and skeletal muscle samples were harvested from the diaphragm, intercostal, biceps femoris, soleus, and trapezius at the time of sacrifice. Following removal of connective tissue and fat, samples were placed in plastic vials and quickly frozen in liquid nitrogen. Sample vials were stored at -70 C for later enzyme and glycogen analysis. Skeletal muscle and liver samples were analyzed for glycogen, succinic dehydrogenase (SDH), phosphofructokinase (PFK), glycogen synthetase (GS), pyruvate dehydrogenase (PDH), and beta-hydroxy acyl CoA dehydrogenase (HAD). The key glucose formation enzymes phosphoenol pyruvate carboxykinase (PEPCK) and fructose-1,6-diphosphatase (F-1,6-DP) were also measured in liver samples. Aortas from the LTDU pigs were removed at sacrifice for determination of lipid infiltration of the arterial wall.

Experimental Procedures

Meal Feeding Test (MFT). Meal feeding tests were conducted in the morning following an overnight fast. MFTs measured the normal hormonal and metabolic responses to eating the Control and LCD chow mixes. Differences in metabolic response were intended to aid in explaining the metabolic adaptations measured by the other testing procedures. Heparin was removed from the lines the night prior to the tests to eliminate its effects on activation of lipoprotein lipase. Blood samples were drawn from the inferior vena cava (IVC) and hepatic portal vein (PV) while the animal remained in its cage or rested quietly in a transport box. These samples were taken 20 minutes prior to feeding (INITIAL) and represented resting measurements of plasma free fatty acids, glucose, lactate, insulin and ketones. Additional resting samples (REST-2) were obtained at 5 minutes prior to feeding the standard morning meal (2% of the body weight). Each animal had been adapted to twice daily feedings of its specific diet (control or LCD) for a total daily intake of 4% of the body weight. Food was offered at zero time, and the pig was given 30 minutes to consume the meal Any food left in the pan was weighed and recorded. Sampling resumed 30 minutes following meal completion. Subsequently, sampling

from both vessels was performed at 60, 90, 120, 150, 180, 210, 240 and 300 minutes following the meal. Samples were immersed in crushed ice and later spun in a refrigerated centrifuge. Plasma was transferred into plastic tubes, then stored at -70 C for later analysis. Metabolite and hormone measurements obtained were expressed as absolute plasma concentrations and as a normalized concentration area. The area under the glucose and insulin curves has been previously used as a means of evaluating the summed response to a glucose challenge (27). The normalized area was derived from a division of the area under the curve by the total test time. This permitted a single comparison of a variable whose value changes over time.

Glucose Tolerance Test (GTT). GTTs were conducted in the morning following an overnight fast to measure hormonal and metabolic responses to a glucose load and as a means of determining any alteration in insulin sensitivity and glucose kinetics resulting from the conditions of the study. GTTs were performed on untrained animals at various times post surgery. Trained animals were administered GTTs during the re-training period and between the weekly runs to exhaustion (RTEs). Animals were placed in a transport cart and then catheter extensions were connected to the IVC and PV catheters. Care was taken to keep the connecting lines, stopcocks and syringes free of contamination. Resting blood samples were obtained 35 and 5 minutes prior to the glucose load. A bolus of glucose (.5g/Kg BW) was rapidly infused into the downstream IVC catheter over a 2-3 minute period. Sampling from the upstream IVC and PV began 2 minutes following completion of glucose infusion. Subsequently, samples were obtained at 6, 10, 15, 20, 30, 40, 50 and 60 minutes post infusion. Samples were immersed in crushed ice and later spun in a refrigerated centrifuge. Plasma was transferred to plastic tubes for storage at -70 C until the time of analysis. Analyses were performed to determine plasma concentrations of insulin, glucose, lactate, free fatty acids and ketones. Both ketones and free fatty acids were measured in baseline samples, while free fatty acids were also measured at 30 and 60 minutes post infusion. Catheter patency was maintained during the study by a slow drip of .9% saline. The area under the glucose curve divided by the area under the insulin curve (27) was used as a measure of insulin sensitivity.

Runs to Exhaustion (RTE). Following satisfactory recovery from surgery and the completion of the re-training protocol, animals performed RTEs to measure moderate intensity exercise endurance on a one time per week schedule. The RTEs on each animal were conducted randomly following either an overnight fast, feeding half of the daily food ration (2% body weight) or administration of intravenous glucose (.5 grams/kg body weight, 4 pigs only). Blood samples were obtained from the IVC and PV for measurements of glucose, lactate and insulin. Ketones and free fatty acids were measured in the IVC only. Samples were obtained just prior to feeding or glucose loading and during a 30 minute period before exercise. Pigs were placed on the treadmill and catheter extensions were connected to each catheter. Care was taken to keep the connecting lines, stopcocks and syringes free of contamination. Catheter patency was maintained as described above. Heart rate was obtained from a surface electrocardiogram while a thermistor inserted into the indwelling temperature port provided continuous measurement of core temperature. Pigs ran at an intensity of 65% of the maximal heart rate reserve until exhausted or the five hour end point had been achieved. Work rates varied from 3.1/5% to 3.5/8%. Treadmill work load was adjusted to achieve the correct heart rate during the first 5 to 10 minutes of exercise and then held constant throughout the remainder of the RTE. Animals rested for five minutes at the end of each hour of running. A 19 inch fan was directed onto the pig from the front of the treadmill and cool water was sprayed on the pig at two to five minute intervals throughout the RTE. Heart rate and core temperature were recorded every five minutes during the RTE. Blood samples were obtained at 5, 10, 40, 60, 90, 120, 150, 180, 210, 240, 270 and 300 minutes of exercise and 7 minutes of recovery. End exercise blood samples, heart rate and core temperatures were obtained prior to 300 minutes, when core temperature exceeded 41 C (106 F), or the animal reached exhaustion. The exhaustion end point was defined as a markedly altered gait and/or failure to maintain the treadmill workload despite repeated negative reinforcement.

Cardiovascular Effects of Pre-Exercise Feeding. Following catheter implantation, animals were allowed to recover and were retrained prior to performing two hour runs under both fasting and pre-feeding conditions. Pigs received one-half of their morning ration of pig chow (1% body weight) at 120 and again at 50 minutes prior to beginning the post-feeding run, while fasting

runs were performed after an overnight fast. Work loads for the two runs were identical and corresponded to an intensity of 65% of the maximal heart rate reserve. Animals ran continuously until 120 minutes or exhaustion defined the end exercise point. Pigs were permitted to recover for a minimum of two days between tests. Radiolabelled microspheres (Ce_{141}, Cr_{51}, Sn_{113}, Ru_{103}, Nb_{95}, Sc_{46}, In_{114} and Gd_{153}) were injected at rest, 5 minutes, 30 minutes and end exercise for measurement of regional blood flow. Blood pressure, heart rate, cardiac output, peripheral resistance, core temperature, arterial and mixed venous blood gases, oxygen consumption, respiratory quotient, and plasma glucose and lactate were determined at rest, 5, 15, 30, 60, 90 and 120 minutes of exercise and at 10 minutes of recovery. Indocyanine green dye (ICG) is cleared exclusively by the liver and its rate of removal is proportional to liver blood flow(32, 38). ICG clearance was measured at rest, 30, 60, and 90 minutes of exercise and during recovery.

Chemical assays. Plasma glucose and lactate were measured on a Yellow Springs Instruments Model 23L glucose/lactate analyzer. Biochemical assays were conducted by collaborating investigators using standard, widely accepted techniques. Details will be published in subsequent reports.

Statistical analysis. Multiple analysis of variance (MANOVA) were performed on the data from the cardiovascular and blood flow distribution studies group of pigs (CHT). Additional single paired and group comparisons were performed using a t test to evaluate possibly significant differences between groups.

Results

Exercise Training Responses. Both LCD and Control trained animals exhibited significant improvements in exercise capacity as evidenced by submaximal and maximal exercise test responses (Table 3, Appendix). Post training responses revealed a greater than 30 b/min reduction in heart rate (HR) at two consistent submaximal work loads as well as a 16-19% increase in the relative watt/pulse (watts/Kg/HR). Peak relative work (watts/Kg) at maximal exercise increased 41% and peak absolute work (watts) increased by 127%, while watts/Kg/HR increased by 44%. Maximal heart rate decreased by 6 b/min following training. Following surgery, recovery and retraining, animals

achieved a trained state comparable to that measured prior to surgery. These training adaptations occurred despite significant weight gains post training (+61% BW) and post surgery (+66% BW) as compared to pre-training weights.

Meal Feeding Tests (MFT). The results of meal feeding tests on LCD and Control animals are listed in Tables 4 and 5, Appendix. Due to the small number of animals, DT and LTDU pigs were combined for comparison with CT animals. No group differences in maximum glucose or area under the glucose curve were observed. Area under the insulin curve and maximum insulin attained were significantly greater for Control than LCD pigs ($p<.05$). Insulin sensitivity, defined as the area under the insulin curve divided by the area under the glucose curve, was also significantly greater for Control than LCD animals (10.7 vs 4.6, $p<.05$).

Runs to Exhaustion (RTE). Data obtained during RTEs are listed in Tables 6-11, Appendix. Six of the ten DT pigs completed a five hour RTE, whereas only two of seven CT pigs completed a five hour run. Selecting the longest RTE performed by each animal for all conditions tested, endurance time was greater for DT than for CT animals (255 ± 62 vs 197 ± 81 min, $p<.01$). A comparison of fasting RTEs revealed a longer run time for the DT than for the CT animals (262 ± 69 vs 199 ± 84 min, $p<.05$). Smaller differences were noted for post-feeding conditions, with both groups containing five animals each (247 ± 50 vs 217 ± 91 min). Two animals from each group performed RTEs after an intravenous glucose load. LCD animals ran longer than Controls following this treatment (240 ± 85 vs 140 ± 28 min).

During fasting RTEs (Tables 6 and 7, Appendix) DT animals exhibited significantly lower IVC lactate concentrations and smaller normalized areas under the lactate curve than for CT pigs ($.83 \pm .48$ vs $2.02 \pm .86$ mmol/L, $p<.005$). The minimum IVC glucose concentrations were higher ($3.0 \pm .7$ vs $2.1 \pm .8$ mmol/L, $p<.005$) and normalized insulin areas lower (3.1 ± 3.2 vs 12.8 ± 10.3 uU/ml, $p<.05$) for the DT than for the CT animals. DT animals had higher resting, maximum and minimum IVC concentrations of ketone bodies than control animals. The ratio of IVC insulin area/glucose area, a measure of insulin sensitivity, was significantly higher for CT than DT pigs (4.0 ± 3.3 vs 2.1 ± 1.0, $p<.05$). CT pigs exhibited a significantly greater normalized PV lactate

area than DT animals under fasting conditions (2.0 ± .8 vs 1.0 ± .4 mmol/L, p<.005).

Following feeding (Tables 8 and 9, Appendix), DT pigs had higher IVC ketone body concentrations at rest and throughout the RTE than CT. IVC insulin for CT was greater than for DT throughout the RTEs. The ratio of IVC insulin area/glucose area was significantly greater for CT than DT animals (3.5 ± 8.5 vs 1.7 ± .1, p<.05). Following glucose infusion (Tables 10 and 11, Appendix), DT animals exhibited higher minimums and larger normalized IVC glucose areas than CT pigs.

Glucose Tolerance Tests (GTT). GTT results were compared for the LCD and control animals. The summarized results of GTTs are presented in Tables 12-17, Appendix for the control untrained (CU), control trained (CT), LCD untrained (DU), LCD trained (DT), long term LCD untrained (LTDU), and combined control and LCD groups, respectively. Preliminary examination of the data suggested no effect of exercise training and animals were separated into LCD or Control groups for comparisons (Table 17, Appendix). DU animals exhibited significantly greater normalized glucose areas (8.5 vs 6.4, p<.05) than CU (Table 14, Appendix). DT normalized glucose area was similarly greater than for CT (Table 15, Appendix). These differences corresponded to nearly equal areas under the insulin curve and was consistent with a lower insulin sensitivity in the LCD groups. For the combined groups (Table 17, Appendix), insulin sensitivity was lower for all LCD than for all control pigs (4.3 vs 6.0, p<.05). However, no significant group differences were observed in maximum insulin, maximum glucose or area under the insulin curve. These data suggest LCD adapted pigs have a reduced insulin sensitivity compared to Controls.

Cardiovascular Effects of Pre-Exercise Feeding. The effects of pre-exercise feeding on hemodynamics, oxygen consumption, metabolites, thermoregulation and regional circulation at rest and during prolonged exercise are shown in Tables 18a, 18b, 19a, and 19b, Appendix, with preliminary feeding vs. fasting group comparison results listed. MANOVA analyses indicated feeding produced higher cardiac outputs(p=.06) and stroke volumes(p=.01), but lower heart rates(p=.06) during the 2 hour runs, with an increase in cardiac output between 5 min and

END (p=.02). The greatest differences occurred at 5-8 min and 15 min of exercise for cardiac output (31.5 and 27.1 ml/kg/min) and stroke volume (.19 and .20 ml/kg/min). Heart rates for the fed condition were approximately 10 b/min lower than for fasting at 15, 30, and 60 minutes of exercise. Mean arterial pressures were similar for the two runs with small increases for fed conditions at 90 min (+5 mmHg) and end exercise (+4 mmHg). Total peripheral resistance was slightly lower for feeding conditions at 5 min (-8%) and 15 min (-7%) of exercise than for fasting, although MANOVA showed no effect of feeding(p=.14). No fasting vs. feeding differences occured for myocardial oxygen consumption as estimated by the product of mean arterial pressure and heart rate (20), with no increase between the 30 min and END time points(MANOVA). Whole body oxygen consumption was marginally higher during the fed runs(p=.10). The largest difference was 2.9 ml/Kg/min (+8%) at 5 min of exercise. Respiratory quotient was higher following feeding for rest and 15 min of exercise. Post-feeding mixed venous lactate was higher at rest but then became progressively lower than fasting concentrations after 15 min of exercise. MANOVA indicated post-feeding exercise lactates were lower than fasting(p=.05), with the largest differences observed at end exercise (1.45 mmol/L, -55%) and in recovery (1.78 mmol/L, -56%). Central body temperature did not differ between feeding and fasting, increased from rest to 30 min (p=.01), and was stable from 30 min to END.

Feeding produced the anticipated increase in resting flows to the distal stomach, duodenum, proximal jejunum and distal jejunum. During exercise feeding resulted in higher flows in some, but not all GI tissues(MANOVA, p<.05). Total gastrointestinal (GI) blood flow was greater for the fed condition (MANOVA, p=.02). These differences amounted to +463, +242, and +206 ml/min or +27, +32, and +21% at rest, 5 min and 30 min of exercise, respectively. There was a decline in total GI flow during exercise(MANOVA, p=.03). Blood flow to the kidneys, spleen, pancreas and liver (arterial only) were not different for the two conditions. Clearance of indocyanine green dye was greater at 60 and 90 min of exercise for post-feeding (MANOVA, p=.05). This confirms the higher total liver (total GI) blood flow for post-feeding conditions as measured by the microsphere technique.

Organ blood flows (OBF) expressed as ml/100 g of tissue are listed in Tables 20a, 20b, 21a, and 21b, Appendix. Transmural myocardial blood flow was higher at rest but lower throughout exercise in the fed condition ($p<.05$). Higher fasting myocardial blood flow was measured in 24 of 24 mean values during exercise, which yields a highly significant chi-square effect of feeding, although the MANOVA showed no effect($p=.30$) due to the small number for that measure($N=4$). Muscle blood flows were higher during exercise in the fasting compared to fed conditions (MANOVA, $p=.04$) in a combined grouping which included soleus, biceps femoris, semitendonosis, and rectus femoris ($N=5$). The differences in flow between conditions occured in face of identical external work loads during the runs. There was no increase in muscle blood flow with time during exercise (MANOVA).

Lipid and Ketone Analysis. Partial data on plasma lipids and ketone bodies are presented in Tables 6-11, Appendix.

Atherosclerosis and general health. The intimal surface of formalin fixed aortas from 5 LTDU pigs were examined for evidence of atherosclerotic changes after Sudan IV staining. No macroscopically visible lipid accumulations were present following over one year of feeding the LCD. This suggests that the LCD is no more atherogenic than standard pig chow. Furthermore, the LCD did not increase blood triglycerides or cholesterol. The LCD pigs were indistinguishable from the control diet pigs in growth rate, appearance, and general health, and there was no evidence of any deleterious effects from long term consumption of the LCD. The LCD pigs were observed to have less body fat than Controls at surgery and necropsy although no measurements were made.

Discussion

Exercise training responses. The ability of the pig to run for extended periods of time (5 Hrs) was important to the design of these studies. In previous work run times were limited due to overheating (3, 4). In our studies overheating was avoided by cooling the exercising pig with water spray and a fan (24). Another contributory factor in the success of the training/testing protocols was that both training and testing were conducted at the same relative moderate intensity exercise(MODX), 65% of VO_2 Max, for each pig. The

cardiovascular and metabolic adaptations of pigs to this type of MODX training has not been previously reported.

Exercise endurance. Exercise endurance in the fasted condition was 63 minutes greater for the DT group than for the CT group. Feeding had no effect on the endurance of either group. Only two animals from each group performed the preexercise glucose load RTEs. However, the CT pigs had much shorter run times after the glucose load than their corresponding fasting or feeding runs, whereas glucose had no effect on DT pigs. The between-group differences in endurance after glucose can be explained by the decreased insulin sensitivity of the LCD pigs. If additional glucose studies confirm the advantage of the LCD adaptation, then a single meal of any composition would apparently have no deleterious effect on MODX performance.

Effects of LCD on metabolism. The results of the MFTs demonstrate the primary stimulus for the metabolic adaptations which occurred as a result of adaptation to the LCD. As expected, eating the LCD provided a lower input of CHO and a markedly lower insulin response than for the control diet. However, the post-feeding glucose was controlled to the same level for both diets. The reduced stimulation of insulin receptors apparently resulted in a decrease in overall insulin sensitivity as measured by the GTTs. Interestingly, the GTTs resulted in insulin responses (normalized areas) that were identical for both groups, while the glucose normalized areas were much greater for the LCD groups. These data suggest a regulatory mechanism which apparently limits the amount of insulin which can be released in response to a glucose challenge. Thus, the control diet pigs suffered much greater metabolic compromise when subjected to the glucose load. It can not be determined from this data whether or not the insulin inhibition of lipase is similarly affected by the adaptive process.

The remarkable differences in metabolism observed between these two diets have interesting implications for man. There may be a gradual variation in glucose/insulin responses which result from variations in dietary carbohydrate intake among individuals. There may additionally be short term disruptions in glucose tolerance which result from short term alterations in diet. The variations in dietary composition between subjects may therefore provide a

major contribution to the observed variations in GTT response (or other metabolic responses) and interactions between preexercise feeding, exercise metabolism, and endurance. The slight decrease in in blood triglyceride and cholesterol concentrations agrees with a previous study in man utilizing a 19% carbohydrate/69% fat diet (36).

There was a significant increase in circulating concentrations of ketone bodies to twice normal. The lower carbohydrate levels (1% of calories) in previous studies (26, 29, 30) resulted in increases of 50-100 times normal. The resting glucose concentrations were higher for the LCD pigs than for control. The previous studies of LCD adaptation have reported lower glucose concentrations than for controls (26, 29, 30). The difference between the current and previous results may be due to the slightly greater CHO content of the diet or due to some metabolic differences between species. In our opinion, the differences are due to the dietary composition and not to physiological differences. The net result of the LCD adaptation on this 7% CHO diet is a slightly increased and more stable blood glucose concentration, a slight elevation in blood ketone body concentration, a decrease in total triglycerides and possibly cholesterol (with exercise training), a decreased sensitivity to CHO in a meal, and no apparent adverse effects on general health or metabolism.

Effects of LCD and exercise on metabolism. The DT pigs exhibited lower lactate concentrations during both fasting and post-feeding RTEs, with higher glucose concentrations during fasting RTEs than CT pigs. Post-feeding RTE insulin concentrations were less for DT than for CT pigs, while both groups had greater concentrations than for the corresponding fasting runs. These data indicate a decline in exercise carbohydrate metabolism as evidenced by higher glucose and lower lactate concentrations for DT pigs under both fasting and post-feeding conditions. The declines in glucose concentrations during the runs in the CT pigs resulted in significantly lower glucose at exhaustion than for LCD pigs. The LCD adaptation appears to preserve available glucose for those organs requiring glucose, such as the central nervous system. Although disputed by some, a previous exercise study (31) reported the development of hypoglycemia and hypoglycemic symptoms associated with long duration exercise. Another study reported a decrement in repetitive motor

performance after induction of hypoglycemia (5). If psychomotor and cognitive function are related to glucose concentration, then the higher and more stable blood glucose observed during RTEs in the DT pigs could translate to better cognitive function during exercise for LCD adapted than for normal diet humans. This preservation of glucose for the central nervous system (and immune system) is the most likely basis for the adaptive response to CHO deprivation. Although ketone bodies were slightly higher in the LCD pigs during RTEs, their concentrations were probably not high enough to have provided significant amounts of energy to tissues.

Effects of feeding and exercise on cardiovascular dynamics. Exercise produced the anticipated increases and decreases in muscle and visceral microsphere blood flows, respectively (3, 4). Feeding resulted in the expected increases in splanchnic organ blood flow (7). The total splanchnic organ blood flows during post-feeding exercise was higher than for fasting at 5 and 30 minutes of exercise.

The elevated splanchnic blood flow (SBF) was confirmed by a more rapid removal of ICG from the circulation during post-feeding exercise. ICG is removed solely by the liver, with removal proportional to total liver blood flow (total SBF) (32, 38). The reduction in the rate ICG removal was similar to that previously reported in man (32, 33). The higher post-feeding total liver blood flows may be primarily responsible for the lower post-feeding exercise blood lactate concentrations due to higher rates of removal. The potential dependency of circulating lactate concentrations on SBF has not been previously reported.

The combined effects of feeding and exercise also resulted in some unanticipated results. Post-feeding exercise resulted in slight elevations in total cardiac output accompanied by significantly greater stroke volume and lower total peripheral resistance. The lower peripheral resistance was presumably due to lower splanchnic organ resistance of significant magnitude to counterbalance the apparent increase in muscle resistance (observed decrease in muscle blood flow). The reduced muscle blood flow observed here during post-feeding exercise corresponded to lower myocardial blood flows in the face of increased cardiac output. The cardiovascular differences were

coincident with higher lactate concentrations during fasting exercise. Higher muscle blood flows and higher mixed venous lactate concentrations suggest that a relationship may exist between local blood flow control and lactate concentration. This will be examined in future analyses. There is also a suggestion of a more complex interrelationship between the presence of food in the gut and both central and peripheral regulation of the cardiovascular system. Stimulation of GI function is known to occur as a result of increased parasympathetic stimulation (17, 28, 39), although many poorly understood local control mechanisms exist in the gut (8, 28, 34, 37). The overall integration of direct neural, neural feedback control to the central nervous system, and local regulatory mechanisms is largely open to question (28, 35). The data suggests a complex feedback control of cardiovascular dynamics modified by elevated parasympathetic activity resultant from the presence of food in the gut which is different from reported gastrointestinal feedbacks (22, 33).

There were no differences in core temperature profiles between the two conditions in the microsphere pigs. The stable core temperatures reported here were also different from the steady increases reported previously by Armstrong (3, 4). The previously reported increase in core temperatures were associated with progressive elevations in muscle blood flows during exercise. The current data do not demonstrate any progression in muscle blood flow after the initial increase at five minutes of exercise. The combined results of these two studies provides a strong argument in favor of increased core temperature positively influencing muscle blood flow and increasing cardiovascular demand.

Summary of significant results.

1. Maximal relative work capacity was increased >40% on the progressive duration moderate intensity exercise protocol used in these studies.

2. Exercise trained pigs were able to run up to five hours at 65% of their heart rate reserve, with body temperatures controlled by water spray and a fan.

3. Moderate intensity exercise endurance was increased an average of 29% over control by adaptation to a low carbohydrate(7% of calories)/high fat(74% of calories) diet (LCD).

4. LCD pigs exhibited a 40% greater glucose and a 59% lower lactate inmixed venous blood during exercise than control diet pigs, suggesting a marked decrease in glucose metabolism.

5. LCD adaptation reduced insulin sensitivity as measured during standard GTTs and during measurement of the metaboilc response to a meal.

6. LCD adaptation resulted in a slight increase blood ketone bodies (2X normal), which was much less than previous reports (50-100X normal) from a lower proportion of carbohydrate (1% of calories) in the diet.

7. The LCD resulted in no increases in blood triglycerides and cholesterol and no evidence of formation of atherosclerotic plaque with long term feeding (>1 year). The LCD pigs were indistinguishable from controls in growth rate, appearance, and behavior.

8. Preexercise feeding resulted in lower myocardial and skeletal muscle blood flows at the same absolute work load than corresponding fasting exercise. These changes were coincident with greater GI blood flow, whole body oxygen consumption, cardiac output, and stroke volume. Lower myocardial blood flows may help explain postprandial angina in man.

9. Preexercise feeding in control diet pigs resulted in lower blood lactate during exercise than corresponding fasting runs, suggesting a greater rate of removal.

Future directions. The above presentation has been brief with limited references to provide expedient dissemination of the available information. As noted in the text, some of the biochemical data are currently being analyzed. Due to the brevity of this report many details were omitted, and except for those reported for the CHT group, statistical analyses were very basic. Detailed discussions of a number of relationships are planned:

1. Relationships among a moderate intensity exercise endurance training protocol, adaptation to a LCD, muscle metabolic enzymes, muscle fatty acid transport capacity (FABP), and availability of blood borne substrates.

2. Correlations among LCD adaptation, substrate availability and utilization, metabolic control mechanisms, and exercise endurance.

3. The effects of preexercise eating on exercise metabolism and cardiovascular dynamics.

4. Development of an integrated protocol for LCD adaptation to maximize efficiency of the adaptive protocol for specific exercise objectives, while minimizing the side effects of CHO deprivation.

5. Development of relationships among central cardiovascular control and local control effects of temperature and blood lactate concentrations.

6. Delineation of the effects of feeding on specific cardiovascular and metabolic variables during exercise (possible relationships with postprandial angina).

7. Establishment of the relationship between total liver blood flow and removal of lactate during exercise.

8. Correlations of catecholamine responses to fasting and post-feeding exercise with cardiovascular, blood flow, and metabolic variables.

9. Correlations of hormonal, cardiovascular, and metabolic variables with control of gastrointestinal blood flow.

10. Integrated applied program of the use low carbohydrate diets and scheduling of meals to improve various types of mission performance.

11. Integration of exercise training responses observed in this study with specific military mission objectives may lead to new insights into the most beneficial exercise protocols for maximization of mission performance.

Acknowledgements

The authors gratefully acknowledge the technical assistance of Robin Giamela, Paul Kelly, Abby Murray, and to the many other University of California, San Diego employees who assisted in this research effort. Special thanks are extended to Susan Soanes for her veterinary and technical support and to M. E. Tumbleson for his advice and consultation in conducting this project.

References

1. Ahlborg G, Felig P. Influence of glucose ingestion on fuel-hormone response during prolonged exercise. Journal of Applied Physiology 1976;41(5):683-688.

2. Ahlborg G, Felig P, Hagenfeldt L, Hendler R, Wahren J. Substrate turnover during prolonged exercise in man. The Journal of Clinical Investigation 1974;53:1080-1090.

3. Armstrong RB, Delp MD, Goljan EF, Laughlin MH. Distribution of blood flow in muscles of miniature swine during exercise. Journal of Applied Physiology 1987;62(3):1285-1298.

4. Armstrong RB, Delp MD, Goljan EF, Laughlin MH. Progressive elevations in muscle blood flow during prolonged exercise in swine. Journal of Applied Physiology 1987;63(1):285-291.

5. Brooke JD, Chapman A, Fisher L, Rosenrot P. Repetitive skill deterioration with fast and exercise-lowered blood glucose. Physiology and Behavior 1982;29(2):245-251.

6. Davies CTM, Thompson MW, Estimated aerobic performance and energy cost of severe exercise of 24 hour duration. Ergonomics 1979; 22:1249-1255.

7. Fara JW. Postprandial mesenteric hyperemia. In: AP Shepherd and DN Granger (Eds), Physiology of the Intestinal Circulation, New York, Raven Press, 1984, 99-106.

8. Fondacaro J. Intestinal blood flow and motility. In: AP Shepherd and DN Granger (Eds), Physiology of the Intestinal Circulation, New York, Raven Press, 1984, 107-120.

9. Galbo H. Pancreatic hormones. In: Hormonal and Metabolic Adaptation to Exercise, New York, Thieme-Stratton, 1983, 30-35.

10. Gray CG. Mechanisms of bioenergetic homeostasis during exercise: a general model. United States-1985. San Diego, California: Naval Health Research Center, Technical Report No. 85-19.

11. Gray CG, Crisman RP, McKirnan MD, White FC. Hepatic portal/systemic vein lactate in exercising swine. Presented at IUPS meeting, 13-19 July 1986 (Abstract).

12. Gray CG, Phillips RW, Tumbleson ME. Mechanisms of bioenergetic homeostasis during exercise: a general model. In: Tumbleson ME (ed), Proceedings of Swine in Biomedical Research, Volume 1, Plenum Publishing Corporation, 1986, 515-532.

13. Gray CG, White FC, Crisman RP, Wisniewski J, McKirnan D, Bloor CM. Chronic swine instrumentation techniques utilizing the Gore-Tex^{tm} peritoneal catheter. United States-1985. San Diego, California: Naval Health Research Center, Technical Report No. 85-16.

14. Gray CG, White FC, Crisman RP, Wisniewski JB, McKirnan MD, Bloor CM. Chronic swine instrumentation techniques utilizing the Gore-Tex^{tm} peritoneal catheter. In: Tumbleson ME (ed), Proceedings of Swine in Biomedical Research, Volume 1, Plenum Publishing Corporation, 1986, 279-290.

15. Gray CG, White FC, McKirnan MD, Bloor CM. Effects of Feeding and Exercise (Ex) on Blood Flow (BF) in Liver (L) and Gastrointestinal Tissues in Swine. Federation Proceedings 1987;46(4):1123 (Abstract).

16. Gray CG, White FC, McKirnan MD, Bloor CM. Exercise (Ex), feeding, gastrointestinal organ blood flow (OBF), and liver oxygen supply in swine. Medicine Science Sports and Exercise 1987;19(2)(Supplement):S80 (Abstract).

17. Guth PH, Leung FW. Physiology of the gastric circulation. In: LR Johnson (Ed), Physiology of the Gastrointestinal Tract, New York, Raven Press, 1987, 1031-1054.

18. Heyman MA, Payne BD, Hoffman JIE, Rudolph AM. Blood flow measurements with radionuclide-labeled particles. Progress in Cardiovascular Disease 1977;20:55-79.

19. Hickson RC, Rennie MJ, Conlee RK, Winder WW, Holloszy JO. Effects of increased plasma fatty acids on glycogen utilization and endurance. Journal of Applied Physiology 1977;43(95):829-833.

20. Kitamura K, Jorgensen CR, Gobel FL, et al. Hemodynamic correlates of myocardial oxygen consumption during upright exercise. Journal of Applied Physiology 1972;32:516-520.

21. Koivisto VA, Karonen S-L, Nikkila EA. Carbohydrate ingestion before exercise: comparison of glucose, fructose, and sweet placebo. Journal of Applied Physiology 1981;51(4):783-787.

22. Longhurst J. Cardiovascular reflexes of gastrointestinal origin. In: AP Shepherd and DN Granger (Eds), Physiology of the Intestinal Circulation, New York, Raven Press, 1984, 165-178.

23. McKirnan MD, Gray CG, Giamela RJ, Buono MJ, Bloor CM. Evidence for splenic contraction in exercising swine. Federation Proceedings 1987; 46(3):679 (Abstract).

24. McKirnan MD, Gray CG, Giamela RJ, Buono MJ, Bloor CM. Skin wetting (SW) reduces core temperature (T) in exercising swine. Physiologist 1986; 29:115 (Abstract).

25. McKirnan MD, Gray CG, White FC, Bloor CM. Swine as a model for studies of gastrointestinal metabolism during acute and chronic exercise. Presented at IUPS meeting, 13-19 July 1986 (Abstract).

26. Miller WC, Bryce GR, Conlee RK. Adaptations to a high-fat diet that increase exercise endurance in male rats. Journal of Applied Physiology 1984;56(1):78-83.

27. Miller WJ, Sherman WM, Ivy JL. Effect of strength training on glucose tolerance and post-glucose insulin response. Medicine and Science in Sports and Exercise 1984;16(6):539-543.

28. Parks DA, Jacobson ED. Mesenteric circulation. In: LR Johnson (Ed), Physiology of the Gastrointestinal Tract, New York, Raven Press, 1987, 1649-1670.

29. Phinney SD, Bistrian BR, Evans WJ, Gervino E, Blackburn GL. The human metabolic response to chronic ketosis without caloric restriction: preservation of submaximal exercise capability with reduced carbohydrate oxidation. Metabolism 1983;32(8):769-776.

30. Phinney SD, Bistrian BR, Wolfe RR, Blackburn GL. The human metabolic response to chronic ketosis without caloric restriction: physical and biochemical adaptation. Metabolism 1983; 32(8):757-768.

31. Pruett EDR. Glucose and insulin during prolonged work stress in men living on different diets. Journal of Applied Physiology 1970; 28(2):199-208.

32. Rowell LB, Blackmon JR, Bruce RA. Indocyanine green clearance and estimated hepatic blood flow during mild to maximal exercise in upright man. Journal of Clinical Investigation 1964;43(8):1677-1690.

33. Rovell LB, Johnson JM. Role of splanchnic circulation in reflex control of the cardiovascular system. In: AP Shepherd and DN Granger (Eds), Physiology of the Intestinal Circulation, New York, Raven Press, 1984, 153-164.

34. Shepherd AP, Granger DN. Metabolic regulation of the intestinal circulation. In: AP Shepherd and DN Granger (Eds), Physiology of the Intestinal Circulation, New York, Raven Press, 1984, 33-48.

35. Solcia E, Capella C, Buffa R, Usellini L, Fiocca R, Sessa F. Endocrine cells of the digestive system. In: LR Johnson (Ed), Physiology of the Gastrointestinal Tract, New York, Raven Press, 1987, 111-130.

36. Thompson PD, Cullinane EM, Eshelman R, Kantor MA, Herbert PN. The effects of high-carbohydrate and high-fat diets on the serum lipid and lipoprotein concentrations of endurance athletes. Metabolism 1984; 33(11):1003-1010.

37. Walsh JH. Gastrointestinal hormones. In: LR Johnson (Ed), Physiology of the Gastrointestinal Tract, New York, Raven Press, 1987, 181-254.

38. Wheeler HO, Cranston WI, Meltzer JI. Hepatic uptake and biliary excretion of indocyanine green in the dog. Proceedings of the Society of Experimental Biology 1958; 99:11-14.

39. Wood JD. Physiology of the enteric nervous system. In: LR Johnson (Ed), Physiology of the Gastrointestinal Tract, New York, Raven Press, 1987, 67-110.

40. Yeager JE, Crisman RP, Sucec AA. The effect of sleep deprivation and moderate intermittent exercise on maximal aerobic capacity. United States-1986. San Diego, California: Naval Health Research Center, Technical Report No. 86-36.

41. Young DR, Pelligra R, Adachi RR. Serum glucose and free fatty acids in man during prolonged exercise. Journal of Applied Physiology 1966; 21(3):1047-1052.

Appendix

Tables 3 through 21b.

Table 3. Exercise Training Responses of Control and LCD Pigs

	Pre-Training	Post-Training	Post-Surgery
STAGE I (3.1 MPH/5% Grade)			
Watts/Kg(Work)	0.68	0.68	0.68
Heart Rate (HR)	211.4 (26.3)	180.0 (28.0)[a]	171.1 (20.0)[a]
HR Delta		-31.1 (25.1)	-35.5 (27.9)
% HR Delta		-14.2 (11.7)	-16.3 (12.1)
Watt Pulse(x100)	3.27 (0.46)	3.86 (0.59)[a]	4.03 (0.49)[a]
% Chng Watt Pulse		18.7 (16.3)	21.8(17.62)
Number	25	25	16
STAGE II (4.3 MPH/5% Grade)			
Watts/Kg(Work)	0.94	0.94	0.94
Heart Rate (HR)	257.2 (28.0)	223.9 (21.3)[a]	219.4 (18.2)[a]
HR Delta		-33.3 (31.5)	-31.0 (29.4)
% HR Delta		-12.1 (11.9)	-16.7 (24.1)
Watt Pulse(x100)	3.74 (0.46)	4.26 (0.44)[a]	4.33 (0.39)[a]
% Chng Watt Pulse		15.8 (16.4)	14.6 (14.1)
Number	25	26	16
STAGE MAXIMUM (Variable)			
Watts/Kg(Work)	2.85 (0.71)	3.91 (0.67)[a]	4.03 (0.70)[a]
Heart Rate (HR)	294.7 (10.9)	288.3 (12.5)[b]	287.1 (10.2)[b]
HR Delta		-5.6 (13.6)	-4.5 (11.3)
% HR Delta		-2.1 (4.9)	-1.6 (3.9)
Watt Pulse(x100)	9.70 (2.48)	13.55 (2.28)[a]	13.99 (2.13)[a]
% Chng Watt Pulse		43.9 (28.2)	43.7 (33.0)
% Chng MAX Rel. Work		40.7 (25.5)	41.2 (31.3)
TOTAL Max Watts	85.2(33.25)	176.7 (41.9)[a]	192.6 (40.2)[a]
% Chng. Total MAX Watts		126.7 (68.6)	138.2 (80.4)
Number	25	25	15

Values presented as Mean (SD). Heart Rate(HR) Delta (HR change), % HR Delta, % Change in Watt Pulse (% Chng), % Change in Maximal (peak) Relative Work Output (% Chng MAX Rel. Work), and % Change in Total (peak absolute) Maximal Work Output (% Chng. Total MAX Watts) are expressed as the difference in comparison to the Pre-training test results; Watt Pulse = Watts/Kg/HR.

[a] = $p<.005$ compared to Pre-Training
[b] = $p<.05$ compared to Pre-Training

Table 4. Hormonal and Metabolic Responses of Control Diet Pigs to a Standardized Control Chow Meal (Meal Feeding Test)

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	83.94	40.78	151.02	52.84	79.89
SD		14.70	108.44	49.09	56.37
N	1	2	2	2	2
IVC FFA (ug FA/ml)	137.98	115.71	238.87	41.77	104.07
SD		97.24	117.70	2.39	10.09
N	1	2	2	2	2
IVC LA (mmol/l)	0.65	0.83	2.50	0.62	1.35
SD	0.39	0.45	1.04	0.29	0.20
N	6	6	6	6	6
IVC Glu (mmol/l)	4.27	4.10	5.68	3.60	4.33
SD	0.45	1.16	1.07	1.27	0.83
N	6	6	6	6	6
IVC INS (uU/ml)	19.02	18.65	117.97	17.47	46.28
SD	24.56	22.78	88.35	8.81	22.77
N	6	6	6	6	6
IVC KET B (mmol/l)	0.03		0.04	0.03	
SD	0.01		0.01	0.01	
N	5		5	5	
PV LA (mmol/l)	0.90	1.07	2.67	1.47	1.22
SD	0.26	0.45	0.31	0.83	0.89
N	3	3	3	3	3
PV INS (uU/ml)	20.50	58.73	216.00	60.50	114.04
SD	6.36	56.56	93.53	42.64	21.97
N	2	3	3	3	2
IVC INS/IVC Glu			19.27	5.97	10.72
SD			12.22	5.06	4.93
N			6	6	6

Mean sample values were obtained when initially (INITIAL) connected to the Inferior Vena Cava (IVC) or Hepatic Portal Vein (PV) catheters and just prior to feeding the meal (REST-2). The maximal (MAX) and minimal (MIN) values during the test and the total area under the curve, with respect to time, were divided by the total time of the test to yield the Normalized area (NORM area). Total Triglycerides (TG) and Total Free Fatty Acids (FFA) are expressed as amounts of FFA per ml of serum (ug FA/ml). Also listed: Lactic Acid (LA); Glucose (Glu); Insulin(INS); Total Ketone Bodies (KET B); Standard Deviation (SD); and Number (N).

Table 5. Hormonal and Metabolic Responses of LCD Adapted Pigs to a Standardized LCD Chow Meal (Meal Feeding Test)

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	130.76	107.54	310.64	81.51	208.00
SD	67.28	92.87	180.38	50.93	107.83
N	4	4	4	4	4
IVC FFA (ug FA/ml)	346.01	472.74	374.19	131.27	250.69
SD	247.56	402.43	269.54	62.01	136.03
N	4	3	4	4	4
IVC LA (mmol/l)	0.58	0.96	1.94	0.62	1.08
SD	0.26	0.70	1.44	0.23	0.47
N	4	5	5	5	5
IVC Glu (mmol/l)	3.90	3.98	4.96	3.84	4.49
SD	0.71	0.43	1.02	0.61	0.91
N	4	5	5	5	5
IVC INS (uU/ml)	7.95	23.72	32.56[b]	10.82	19.91[b]
SD	3.89	32.77	20.62	2.44	9.52
N	2	5	5	5	5
IVC KET B (mmol/l)	0.05		0.06	0.05[b]	
SD	0.02		0.03	0.02	
N	4		4	4	
PV LA (mmol/l)	0.85	0.85	2.90	0.95	1.52
SD	0.35	0.07	2.26	0.21	0.72
N	2	2	2	2	2
PV INS (uU/ml)	40.00	12.50	47.00	15.50	28.19[b]
SD		6.36	2.83	3.54	1.92
N	1	2	2	2	2
IVC INS/IVC Glu			6.81[b]	2.86	4.59[b]
SD			4.84	0.70	2.60
N			5	5	5

Note: See Table 4 for explanation of abbreviations.

[a] = p<.005 compared to the control Meal Feeding Test(MFT)
[b] = p<.05 compared to the control MFT

Table 6. Fasting Control Pigs' Metabolic and Hormonal Responses to a Run to Exhaustion (RTE) at 65% of Heart Rate Reserve

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)		63.33	99.95	66.31	82.75
SD		43.15	45.38	40.09	43.75
N	0	4	4	4	4
Free Chol (ug/.5ml)		42.90	57.30	44.10	
SD		14.00	0.42	7.21	
N	0	2	2	2	
IVC FFA (ug FA/ml)		69.01	693.22	153.18	306.20
SD		35.14	233.05	83.90	23.26
N	0	2	2	2	2
IVC LA (mmol/l)		0.66	4.08	0.88	2.02
SD		0.29	2.08	0.39	0.86
N	0	12	12	12	12
IVC Glu (mmol/l)		3.93	4.53	2.13	3.34
SD		0.54	1.18	0.79	0.87
N	0	12	12	12	12
IVC INS (uU/ml)		12.07	23.38	4.32	12.84
SD		8.26	28.57	1.55	10.29
N	0	12	12	12	12
IVC KET B (mmol/l)		0.03	0.09	0.03	
SD		0.01	0.02	0.01	
N	0	9	9	9	
PV LA (mmol/l)		0.73	3.60	0.87	1.99
SD		0.34	1.98	0.42	0.82
N	0	6	6	6	6
PV INS (uU/ml)		33.85	41.80	6.22	18.93
SD		51.06	24.59	2.91	13.06
N	0	6	6	6	6
IVC INS/IVC Glu			5.84	2.20	3.98
SD			7.89	1.02	3.32
N		0	12	12	12

Note: See Table 4 for explanation of abbreviations.

Table 7. Fasting LCD Adapted Pigs' Metabolic and Hormonal Responses to a Run to Exhaustion (RTE) at 65% of Heart Rate Reserve

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	59.00	88.30	119.03	62.60	88.90
SD		62.51	53.17	30.83	39.05
N	1	5	7	7	7
Free Chol (ug/.5ml)	66.60	50.40	69.60	36.00	
SD			16.97	10.18	
N	1	1	2	2	
IVC FFA (ug FA/ml)		386.02	882.85	336.68	509.10
SD		361.75	515.47	285.59	269.11
N	0	4	5	5	5
IVC LA (mmol/l)	0.60	0.75	1.83[a]	0.44[a]	0.83[a]
SD		0.31	1.48	0.20	0.48
N	1	18	19	19	19
IVC Glu (mmol/l)	3.40	3.98	4.47	2.99[a]	3.64
SD		0.27	0.73	0.67	0.52
N	1	18	19	19	19
IVC INS (uU/ml)	10.00	10.23	17.78	4.92	8.06[b]
SD		6.41	13.47	1.81	3.18
N	1	18	19	19	18
IVC KET B (mmol/l)		0.05[b]	0.14[b]	0.06[a]	
SD		0.02	0.04	0.01	
N	0	3	3	3	
PV LA (mmol/l)		0.74	1.83[b]	0.62	1.00[a]
SD		0.39	1.40	0.27	0.43
N	0	10	11	11	10
PV INS (uU/ml)		23.36	43.36	6.35	13.46
SD		26.99	46.59	4.66	7.10
N	0	10	11	11	9
IVC INS/IVC Glu			4.15	1.66[b]	2.31[b]
SD			3.30	0.53	0.84
N		0	19	19	17

Note: See Table 4 for explanation of abbreviations.

[a] = $p<.005$ compared to control Fasting RTE
[b] = $p<.05$ compared to control Fasting RTE

Table 8. Post-feeding Control Pigs' Metabolic and Hormonal Responses to a Run to Exhaustion (RTE) at 65% of Heart Rate Reserve

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	142.83	88.75	236.38[b]	99.21	159.85
SD					
N	1	1	1	1	1
IVC FFA (ug FA/ml)	53.73	50.21	547.90	199.32	358.35
SD					
N	1	1	1	1	1
IVC LA (mmol/l)	1.08	1.50[a]	2.83	1.25	1.79
SD	0.22	0.73	1.77	0.85	1.25
N	5	6	6	6	6
IVC Glu (mmol/l)	4.34	4.48	5.18	3.00	4.09
SD	0.34	1.42	0.78	1.31	0.86
N	5	6	6	6	6
IVC INS (uU/ml)	8.72	48.47[a]	31.62	8.03	15.31
SD	3.46	23.83	14.01	6.91	8.49
N	5	6	6	6	6
IVC KET B (mmol/l)	0.03	0.04[b]	0.08	0.04[b]	
SD	0.004	0.01	0.03	0.01	
N	5	6	6	6	
PV LA (mmol/l)	1.10	1.45[b]	2.50	1.35	1.11
SD		0.07	1.41	0.49	1.56
N	1	2	2	2	2
PV INS (uUml)	61.00	82.20	63.90	7.15	12.19
SD		49.78	4.10	2.62	14.47
N	1	2	2	2	2
IVC INS/IVC Glu			6.18	2.49	3.53
SD			3.04	1.36	1.35
N		0	6	6	6

Note: See Table 4 for explanation of abbreviations.

[a] = p<.005 compared to control Fasting RTE
[b] = p<.05 compared to control Fasting RTE

Table 9. Post-feeding LCD Adapted Pigs' Metabolic and Hormonal Responses to a Run to Exhaustion (RTE) at 65% of Heart Rate Reserve

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	72.80	174.40	242.20	119.69	188.88
SD			79.76	39.02	31.06
N	1	1	2	2	2
IVC FFA (ug FA/ml)	216.47	89.85	277.24[d]	159.60[d]	232.28[d]
SD	80.51	127.07	22.40	3.25	5.75
N	2	2	2	2	2
IVC LA (mmol/l)	0.60[c]	0.98[a]	2.58	0.83[a]	1.16[a]
SD	0.20	0.25	1.81	0.34	0.45
N	6	5	6	6	5
IVC Glu (mmol/l)	4.38[b]	4.40	5.02[b]	3.08	3.96
SD	0.55	0.61	0.66	0.48	0.14
N	6	5	6	6	5
IVC INS (uU/ml)	10.70	26.40[a]	18.03[c]	4.58[b]	6.94[d]
SD	1.86	19.52	16.33	1.82	1.74
N	6	5	6	6	5
IVC KET B (mmol/l)	0.05[c]	0.06[d]	0.16[bc]	0.09[bd]	
SD	0.01	0.01	0.03	0.05	
N	4	3	4	4	
PV LA (mmol/l)	0.60[c]	1.13[b]	3.00	0.88[a]	1.02
SD	0.10	0.31	1.92	0.59	1.06
N	3	3	4	4	3
PV INS (uU/ml)	74.53	29.77[b]	45.25	5.23	8.01
SD	71.29	15.88	45.90	1.40	6.63
N	3	3	4	4	3
IVC INS/IVC Glu			3.63	1.46[b]	1.75[bd]
SD			3.34	0.42	0.42
N		0	6	6	5

Note: See Table 4 for explanation of abbreviations.

[a] = p<.005 compared to LCD fasting RTE
[b] = p<.05 compared to LCD fasting RTE
[c] = p<.005 compared to control post-feeding RTE
[d] = p<.05 compared to control post-feeding RTE

Table 10. Post-glucose Infusion Control Pigs' Metabolic and Hormonal to a Run to Exhaustion (RTE) at 65% of Heart Rate Reserve

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	80.60		123.70	58.60	66.79
SD					
N	1	0	1	1	1
Free Chol (ug/.5ml)	60.20		75.00	66.00	
SD					
N	1	0	1	1	
IVC LA (mmol/l)	0.50	1.50	2.05	0.65	1.20
SD	0.28	0.28	1.06	0.21	0.19
N	2	2	2	2	2
IVC Glu (mmol/l)	3.55	9.25	5.50	1.60	2.71
SD	0.07	2.76	1.70	0.57	1.24
N	2	2	2	2	2
IVC INS (uU/ml)	10.00	67.00	35.50	7.00	16.12
SD			17.68	1.41	1.04
N	1	1	2	2	2
PV LA (mmol/l)	0.50	1.50	2.30	0.50	1.30
SD					
N	1	1	1	1	1
PV INS (uU/ml)	13.00	140.00	81.00	4.00	18.73
SD					
N	1	1	1	1	1
IVC INS/IVC Glu			7.30	4.50	6.56
SD			5.47	0.71	2.62
N		0	2	2	2

Note: See Table 4 for explanation of abbreviations.

Table 11. Post-glucose Infusion LCD Adapted Pigs' Metabolic and Hormonal Responses to a RTE at 65% of Heart Rate Reserve

	INITIAL	REST-2	MAX	MIN	NORM Area
IVC TG (ug FA/ml)	154.50	115.35	240.25	66.90	122.57
SD	16.97	5.87	51.97	18.24	3.07
N	2	2	2	2	2
Free Chol (ug/.5ml)	50.40	75.00	66.00	40.80	
SD					
N	1	1	1	1	
IVC FFA (ug FA/ml)	1835.8	1412.00	1728.20	1373.40	1930.70
SD					
N	1	1	1	1	1
IVC LA (mmol/l)	0.85	0.70	0.95	0.55	0.71
SD	0.21	0.28	0.21	0.21	0.33
N	2	2	2	2	2
IVC Glu (mmol/l)	4.15	10.45	6.55	3.05	3.76
SD	0.49	1.06	0.21	0.21	0.44
N	2	2	2	2	2
IVC INS (uU/ml)	21.50	73.00	52.00	6.00	79.04
SD	17.68		12.73	1.41	
N	2	1	2	2	1
PV LA (mmol/l)		1.00	1.50	0.80	1.23
SD					
N	0	1	1	1	1
PV INS (uU/ml)	7.00	126.00	173.00	7.00	79.50
SD					
N	1	1	1	1	1
IVC INS/IVC Glu			7.97	1.96	22.91
SD			2.20	0.33	
N		0	2	2	1

Note: See Table 4 for explanation of abbreviations.

Table 12. Control Untrained Pigs' Responses to an Intravenous Glucose Tolerance Test

PIG #	INITIAL INSULIN	MAX GLUCOSE	MAX INSULIN	N. AREA GLUCOSE	N. AREA INSULIN	INSULIN SENSITIVITY
21	5.5	16.0	40.1	6.5	23.6	3.8
23	7.7	15.1	65.4	7.4	30.8	4.2
35	4.2	13.4	65.1	5.2	33.9	6.8
22	3.6	14.1	121.1	6.5	78.0	12.0
79	79.0	12.2	50.0	6.5	29.7	4.6
MEAN	20.0	14.2	68.3	6.4	39.2	6.3
SD	33.0	1.5	31.4	0.8	22.0	3.4

Note: See Table 4 for explanation of abbreviations.

Table 13. Control Trained Pigs' Responses to an Intravenous Glucose Tolerance Test

PIG #	INITIAL INSULIN	MAX GLUCOSE	MAX INSULIN	N. AREA GLUCOSE	N. AREA INSULIN	INSULIN SENSITIVITY
178	6.4	16.1	121.8	6.0	36.6	6.1
195	4.0	15.7	32.0	6.2	14.0	2.3
214	10.0	18.1	81.0	6.4	36.3	5.7
237	4.1	15.9	88.6	6.8	43.3	6.4
239	4.5	17.3	93.5	4.9	44.2	9.1
119	8.0	15.9	53.0	5.8	27.4	4.7
MEAN	6.2	16.5[a]	78.3	6.0	33.6	5.7
SD	2.4	1.0	31.7	0.7	11.4	2.2

Note: See Table 4 for explanation of abbreviations.

[a] = $p<.005$ compared to control untrained GTTs

Table 14. LCD Untrained Pigs' Responses to an Intravenous Glucose Tolerance Test

PIG #	INITIAL INSULIN	MAX GLUCOSE	MAX INSULIN	N. AREA GLUCOSE	N. AREA INSULIN	INSULIN SENSITIVITY
22	5.3	14.5	60.4	6.9	44.0	6.4
24	5.1	15.9	34.8	10.5	23.4	2.2
76	82.0	16.0	92.0	9.5	35.3	3.7
79	54.0	14.0	117.0	8.7	29.7	3.4
215	14.2	16.5	63.0	6.7	30.0	4.5
MEAN	32.1	15.4	73.4	8.5[b]	32.5	4.1
SD	34.4	1.1	31.7	1.6	7.7	1.5

Note: See Table 4 for explanation of abbreviations.

[b] = $p<.05$ compared to control untrained GTTs

Table 15. LCD Trained Pigs' Responses to an Intravenous Glucose Tolerance Test

PIG #	INITIAL INSULIN	MAX GLUCOSE	MAX INSULIN	N. AREA GLUCOSE	N. AREA INSULIN	INSULIN SENSITIVITY
151	6.5	15.7	61.0	7.2	33.3	4.6
179	8.6	15.8	57.6	10.0	39.4	3.9
196	9.0	15.6	67.0	6.7	28.1	4.2
271	9.0	14.8	87.1	8.0	49.6	6.2
321	12.0	18.5	70.5	7.9	41.2	5.3
340	12.0	18.1	71.0	6.7	33.7	5.0
89	6.0	15.3	48.0	9.1	34.6	3.8
MEAN	9.0[b]	16.3	66.0	7.9[a]	37.1	4.7
SD	2.4	1.4	12.3	1.2	7.0	0.9

Note: See Table 4 for explanation of abbreviations.

[a] = $p<.005$ compared to control trained GTTs
[b] = $p<.05$ compared to control trained GTTs

NO Differences compared to LCD untrained GTTs

Table 16. Long Term LCD Untrained Pigs' Responses to an Intravenous Glucose Tolerance Test

PIG #	INITIAL INSULIN	MAX GLUCOSE	MAX INSULIN	N. AREA GLUCOSE	N. AREA INSULIN	INSULIN SENSITIVITY
152	15.0	15.4	78.0	9.8	54.3	5.6
190	9.0	17.6	60.0	7.7	22.6	2.9
194	7.0	16.4	41.0	7.5	23.9	3.2
213	8.1	15.7	62.2	5.7	27.1	4.8
227		18.9	61.0	11.8	36.3	3.1
MEAN	9.8	16.8[a]	60.4	8.5[b]	32.8	3.9
SD	3.6	1.4	13.1	2.4	13.1	1.2

Note: See Table 4 for explanation of abbreviations.

[a] = $p<.005$ compared to control untrained GTTs
[b] = $p<.05$ compared to control untrained GTTs

Table 17. Summary of Responses of All LCD Pigs Compared to All Control Pigs to an Intravenous Glucose Tolerance Test

PIG #	INITIAL INSULIN	MAX GLUCOSE	MAX INSULIN	N. AREA GLUCOSE	N. AREA INSULIN	INSULIN SENSITIVITY
ALL CONTROL (CU + CT, N = 11)						
MEAN	12.5	15.4	73.8	6.2	36.2	6.0
SD	22.2	1.7	30.4	0.7	16.3	2.7
ALL LCD (DU + DT + LTDU, N = 17)						
MEAN	16.4	16.2	66.6	8.3[a]	34.5	4.3[b]
SD	21.0	1.4	19.4	1.6	9.0	1.2

Note: See Table 4 for explanation of abbreviations.

[a] = $p<.005$ compared to all control GTTs
[b] = $p<.05$ compared to all control GTTs

Table 18a. Fasting cardiovascular, metabolic, and thermal responses of control trained pigs to 2-hour runs at 65% of heart rate reserve

PARAMETER	REST	5'	15'	30'	60'	90'[4]	END	Recvy
Total Cardiac Output (l/min)	6.00 (1.01)	13.34 (2.26)	14.03 (2.10)	14.53 (2.17)	15.18 (2.76)	15.85 (2.87)	15.35 (3.08)	
CO [Relative] (ml/min/Kg)	129.61 (43.53)	279.84 (47.31)	285.66 (62.88)	292.45 (47.86)	305.21 (57.33)	298.51 (59.08)	307.04 (53.03)	
Stroke Volume (ml)	63.36 (14.21)	63.78 (13.75)	65.23 (12.39)	64.73 (10.31)	66.21 (11.81)	67.58 (9.97)	64.23 (12.55)	
Stroke Vol [Relative] (ml/Kg)	1.35 (0.39)	1.33 (0.21)	1.31 (0.24)	1.30 (0.22)	1.33 (0.25)	1.28 (0.25)	1.29 (0.23)	
$V.O_2$ (ml/min)	403.11 (108.50)	1613.18 (384.57)	1671.99 (339.29)	1668.08 (307.12)	1736.10 (342.15)	1778.87 (390.41)	1733.41 (407.19)	
$V.O_2$ [Relative] (ml/min/Kg)	8.52 (2.96)	33.10 (3.87)	33.60 (6.91)	33.23 (4.51)	34.70 (5.89)	33.03 (5.31)	34.31 (5.41)	
$V.CO_2$ (ml/min)	324.92 (74.20)	1545.76 (439.46)	1344.92 (430.14)	1602.94 (375.02)	1401.41 (237.33)	1463.45 (381.12)	1516.16 (455.93)	
Resp. Quotient	0.82 (0.15)	0.95 (0.11)	0.79 (0.16)	0.97 (0.18)	0.81 (0.09)	0.83 (0.15)	0.87 (0.11)	
Lactate (mmol/l)	0.66 (0.30)	1.73 (0.94)	1.76 (1.18)	1.68 (1.14)	1.48 (1.05)	1.80 (1.62)	2.08 (1.62)	2.50 (2.88)
Core Temp (deg F)	101.40 (0.47)	102.72 (1.16)	103.70 (1.26)	103.78 (1.25)	103.53 (1.32)	103.27 (1.21)	103.33 (1.06)	103.61 (1.59)
Heart Rate	97.37 (19.47)	210.89 (13.47)	216.63 (13.95)	225.38 (14.59)	229.50 (12.42)	233.67 (9.48)	234.14 (9.87)	133.63 (14.99)
Mean BP (mm Hg)	107.44 (12.51)	125.56 (17.39)	125.00 (14.61)	123.25 (15.92)	121.25 (13.75)	119.33 (13.49)	117.00 (11.19)	113.50 (13.61)
BP X HR/1000	10.61 (3.09)	26.48 (3.96)	27.14 (4.13)	27.80 (4.27)	27.82 (3.51)	27.87 (3.24)	27.55 (3.30)	15.21 (2.67)
Total Periph. Resistance	18.43 (3.99)	9.73 (2.43)	9.14 (2.00)	8.75 (2.29)	8.35 (2.43)	7.78 (1.73)	8.00 (2.33)	

Values presented as mean (SD) with N=9 at rest and 5', and N=8 for others unless noted. [4] N=6.
Abbreviations: Organ blood flows (OBFs) listed for spleen (SPL), pancreas (PNC), combined stomach and intestines (GI), and liver (LIV). OBFs are listed as total organ flows (ml/min)/Kg body weight. Cardiac Output (CO), oxygen uptake ($V.O_2$), carbon dioxide output ($V.CO_2$), Indocyanine Green (ICG) removal constant (k) and ICG half-life (ICG t 1/2), blood pressure (BP) and other measures listed were obtained at Rest, while exercising up to END, and post-exercise (Recvy).

Table 18b. Fasting summary of gastrointestinal organ blood flow responses of control trained pigs to 2-hour runs at 65% of heart rate reserve

PARAMETER	REST	5′	15′	30′	60′	90′	END	Recvy
GI % of Tot CO (%)	22.21 (8.11)	3.72 (2.16)[4]		5.06 (1.80)			3.78 (1.00)[4]	
ICG k (X 10)	-1.19 (0.33)[1]			-0.97 (0.23)[2]	-0.79 (0.25)	-0.82 (0.19)[3]		-0.78 (0.24)[2]
ICG t 1/2 (min)	6.17 (1.52)[1]			7.46 (1.67)[2]	9.83 (3.92)	8.79 (2.28)[3]		9.70 (3.47)[2]
Organ Blood Flows (ml/min/Kg BW):								
SPL	4.21 (2.30)	1.01 (1.37)[4]		0.85 (0.53)			0.35 (0.45)[4]	
PNC + GI	19.13 (8.67)	7.22 (5.77)[4]		12.48 (7.19)			8.17 (3.35)[4]	
SPL + PNC + GI	23.34 (8.51)	8.24 (5.89)[4]		13.33 (7.12)			8.52 (3.67)[4]	
LIV	1.64 (1.23)	1.69 (1.59)[4]		1.48 (0.85)			2.89 (0.55)[4]	
SPL+PNC+GI+LIV	24.99 (9.07)	9.93 (6.82)[4]		14.81 (7.32)			11.41 (4.05)[4]	

Values presented as Mean (SD) with N=7 unless otherwise noted. [1] N=9; [2] N=8; [4] N=6; [6] N=3
NOTE: See Table 18a for abbreviations.

Table 19a. Post-feeding cardiovascular, metabolic, and thermal responses of control trained pigs to 2-hour runs at 65% of heart rate reserve

PARAMETER	REST	5′	15′	30′	60′[2]	90′[3]	END[2]	Recvy[2]
Total Cardiac Output (l/min)	6.39 (1.02)	14.79 (2.68)	14.99 (2.91)	14.88 (2.96)	15.51 (3.55)	15.85 (4.05)	16.18 (3.71)	
CO [Relative] (ml/min/Kg)	137.44 (40.30)	311.37 (63.59)	312.79 (52.22)	311.76 (58.65)	307.15 (43.57)	314.59 (53.01)	320.43 (46.63)	
Stroke Volume (ml)	66.89 (14.39)	73.06 (16.95)	72.84 (15.69)	69.83 (15.36)	71.10 (16.45)	70.16 (17.55)	70.91 (16.89)	
Stroke Vol [Relative] (ml/Kg)	1.39 (0.23)	1.52[c] (0.26)	1.51[c] (0.21)	1.46 (0.25)	1.41 (0.22)	1.40 (0.25)	1.42 (0.26)	
$V.O_2$ (ml/min)	430.40 (82.49)	1741.62 (423.81)	1758.86 (426.28)	1695.70 (396.32)	1793.09 (451.10)	1815.59 (495.90)	1857.46 (465.79)	
$V.O_2$ [Relative] (ml/min/Kg)	9.09 (2.03)	36.05 (5.92)	36.18 (4.57)	35.01 (4.76)	35.29 (4.31)	35.74 (4.59)	36.46 (3.76)	
$V.CO_2$ (ml/min)	431.66[a] (80.12)	1704.11 (419.42)	1623.19 (475.78)	1486.56 (320.46)	1465.49 (312.96)	1545.45 (436.63)	1479.29 (438.68)	
Resp. Quotient	1.01[a] (0.11)	0.98 (0.05)	0.92[b] (0.08)	0.89 (0.11)	0.83 (0.08)	0.86 (0.12)	0.80 (0.13)	
Lactate (mmol/l)	0.98[a] (0.16)	1.99 (0.77)	1.57 (0.59)	1.31 (0.39)	1.00 (0.40)	0.86 (0.55)	1.01[c] (0.59)	1.26 (0.63)
Core Temp (deg F)	101.56 (0.80)	103.00 (0.52)	103.42 (0.98)	103.32 (0.94)	103.38 (0.90)	103.24 (1.06)	103.53 (0.37)	102.46[c] (0.63)
Heart Rate	97.56 (18.44)	204.67 (18.38)	206.67[c] (12.64)	213.89[c] (11.01)	218.13[b] (10.25)	225.43[c] (9.78)	229.00 (13.20)	129.13 (32.84)
Mean BP (mm Hg)	112.33 (17.04)	129.11 (19.51)	127.00 (15.80)	127.67 (16.50)	122.75 (15.05)	124.00 (12.44)	121.00 (11.06)	117.75 (11.71)
BP X HR/1000	11.14 (3.74)	26.53 (5.25)	26.29 (4.02)	27.36 (4.31)	26.84 (4.15)	28.02 (3.75)	27.98 (4.02)	15.29 (4.44)
Total Periph. Resistance	17.98 (3.82)	9.01 (2.22)	8.81 (2.30)	8.94 (2.41)	8.32 (2.28)	8.29 (2.32)	7.90 (2.31)	

Values presented as Mean (SD) with N=9 unless otherwise noted. [2] N=8; [3] N=7
Note: See Table 18a for Abbreviations. Significance levels compared to Fasting are:

[a] = $p<.005$; [b] = $p<.05$; [c] = $p<.01$

Table 19b. Post-feeding summary of gastrointestinal organ blood flow response of control trained pigs to 2-hour runs at 65% of heart rate reserve.

PARAMETER	REST	5′	15′	30′	60′	90′	END	Recvy
GI % of Tot CO (%)	28.32 (7.88)	4.96 (0.93)		6.31[c] (0.71)			3.92 (1.10)	
IOG k (X 10)	-1.17 (0.43)[1]			-0.97 (0.16)	-0.96[c] (0.19)	-0.93 (0.09)[5]		-0.70 (0.17)[2]
IOG t 1/2 (min)	7.04 (4.00)[1]			7.31 (1.26)	7.50[c] (1.57)	7.52 (0.79)[5]		10.83 (4.32)[2]
Organ Blood Flows (ml/min/kg BW):								
SPL	4.33 (1.41)	0.75 (0.80)		1.12 (1.09)			0.51 (0.39)	
PNC + GI	28.67[c] (11.87)	11.55[c] (3.40)		14.44 (5.64)			9.44 (3.74)	
SPL+PNC+GI	32.99[c] (11.68)	12.23[c] (2.92)		15.56 (5.40)			9.94 (3.81)	
LIV	1.49 (1.50)	2.13 (1.81)		3.03 (2.94)			2.35 (2.39)	
SPL+PNC+GI+LIV	34.38[c] (11.90)	14.36[c] (2.78)		18.59 (3.74)			12.30 (4.26)	

Values presented as Mean (SD) with N=7 unless otherwise noted. [1] N=9; [2] N=8; [5] N=5.
Note: See Table 18a for abbreviations. Significance levels compared to Fasting are:

[a] = p<.005; [b] = p<.05; [c] = p<.01

Table 20a. Fasting Organ Blood Flows of control trained pigs during 2-hour runs at heart rate reserve

ORGAN (ml/gm/min)	REST	5′	30′	END EX
RT. KIDNEY	4.19 ± 0.85(7)	3.42 1.42(5)	3.67 0.81(7)	2.34 1.24(6)
LT. KIDNEY	4.21 ± 0.86(7)	3.35 1.35(5)	3.42 0.80(7)	2.31 1.27(6)
ADRENAL	1.57 ± 1.19(6)	2.63 1.28(4)	3.08 1.72(6)	2.76 1.24(5)
RT. BRAIN	0.84 ± 0.26(4)	0.67 0.31(4)	0.61 0.27(4)	0.75 0.55(4)
LT. BRAIN	0.84 ± 0.35(4)	0.71 0.33(4)	0.65 0.25(4)	0.76 0.51(4)
RT. LUNG	0.47 ± 0.33(6)	0.73 0.65(4)	1.86 1.50(6)	1.74 1.67(5)
LT. LUNG	0.38 ± 0.24(6)	0.44 0.20(4)	1.47 1.22(6)	1.53 1.79(5)
STOMACH proximal	0.20 ± 0.12(7)	0.13 0.08(5)	0.11 0.04(7)	0.10 0.05(6)
STOMACH distal	0.43 ± 0.27(7)	0.14 0.12(5)	0.32 0.32(7)	0.23 0.25(6)
DUODEUM	0.85 ± 0.53(7)	0.33 0.14(5)	0.48 0.25(7)	0.47 0.37(6)
JEJUNUM proximal	0.68 ± 0.30(7)	0.33 0.18(5)	0.42 0.24(7)	0.33 0.19(6)
JEJUNUM distal	0.52 ± 0.31(7)	0.27 0.12(5)	0.41 0.34(7)	0.24 0.09(6)
ILEUM proximal	0.71 ± 0.47(7)	0.37 0.31(5)	0.43 0.38(7)	0.27 0.13(6)
ILEUM distal	0.56 ± 0.35(7)	0.24 0.14(5)	0.38 0.33(7)	0.24 0.12(6)
COLON proximal	0.49 ± 0.20(7)	0.30 0.17(5)	0.34 0.11(7)	0.24 0.12(6)
COLON distal	0.33 ± 0.12(7)	0.19 0.07(5)	0.23 0.09(7)	0.15 0.07(6)
SPLEEN	2.01 ± 1.17(7)	0.56 0.64(5)	0.40 0.25(7)	0.16 0.22(5)
PANCREAS	1.51 ± 0.76(7)	0.44 0.29(5)	0.74 0.28(7)	0.34 0.31(6)
LIVER	0.08 ± 0.05(7)	0.10 0.08(5)	0.07 0.04(7)	0.14 0.04(5)

Values presented as Mean ± SD(N)

Table 20b. Fasting Organ Blood Flows of controled trained pigs during 2-hour runs at 65% heart rate reserve

ORGAN (ml/gm/min)	REST	5'	30'	END EX
HEART:				
R Vent-epicardium(epi)	1.00 ± 0.03(4)	2.76 1.30(4)	2.80 0.77(4)	3.59 0.65(4)
R Vent-endocardium(endo)	1.11 ± 0.21(4)	3.38 1.76(4)	3.35 0.82(4)	4.00 0.83(4)
L Vent-epi	1.07 ± 0.07(4)	2.28 0.83(4)	2.61 0.73(4)	3.27 0.89(4)
L Vent-endo	1.25 ± 0.12(4)	2.84 1.28(4)	2.89 0.71(4)	3.06 0.37(4)
L Vent-mid	1.27 ± 0.18(4)	2.77 1.21(4)	3.00 0.78(4)	3.54 0.68(4)
SEPTUM-epi	1.22 ± 0.07(4)	2.94 1.07(4)	3.00 0.98(4)	3.64 0.82(4)
SEPTUM-endo	1.18 ± 0.07(4)	3.20 1.49(4)	3.11 1.05(4)	3.28 0.40(4)
SEPTUM-mid	1.29 ± 0.10(4)	2.80 0.98(4)	3.11 0.97(4)	3.64 0.61(4)
SKELETAL MUSCLES:				
R Diaphragm	0.23 ± 0.10(4)	0.50 0.08(4)	0.60 0.30(4)	0.92 0.81(4)
L Diaphragm	0.23 ± 0.08(4)	0.51 0.13(4)	0.64 0.38(4)	0.97 0.72(4)
Trapezius	0.19 ± 0.07(4)	0.88 0.38(4)	0.94 0.43(4)	1.04 0.52(4)
R Tricepts Lng Hd	0.15 ± 0.12(4)	0.85 0.43(4)	0.69 0.38(4)	0.80 0.48(4)
R Brachialis	0.22 ± 0.04(3)	1.77 0.61(4)	1.80 0.54(4)	1.91 0.73(4)
R Soleus	0.15 ± 0.06(7)	0.46 0.24(5)	0.65 0.15(7)	0.65 0.23(6)
R Biceps Fem	0.14 ± 0.10(7)	1.01 0.37(5)	1.08 0.21(7)	1.11 0.30(6)
R Semitendinosis	0.14 ± 0.14(7)	0.65 0.32(5)	0.51 0.20(7)	0.58 0.25(6)
R Rectus Femoris	0.08 ± 0.06(7)	1.09 0.53(5)	0.84 0.45(7)	0.99 0.46(6)
R Tibialis Ant	0.09 ± 0.06(5)	1.39 0.44(5)	1.29 0.60(7)	1.29 0.41(6)
R Intercostal	0.09 ± 0.04(4)	0.30 0.07(4)	0.31 0.07(4)	0.41 0.11(4)
R Lats	0.06 ± 0.05(4)	0.31 0.18(4)	0.22 0.11(4)	0.24 0.15(4)
Ventral Neck	0.13 ± 0.12(4)	0.43 0.33(4)	0.38 0.29(4)	0.61 0.29(4)
Cremaster	0.11 ± 0.09(7)	0.15 0.13(4)	0.22 0.14(6)	0.46 0.34(5)

Values presented as Mean ± SD(N)

Table 21a. Post-feeding Organ Blood Flows of Control Trained pigs during 2-hour runs at 65% of Heart Rate Reserve

ORGAN (ml/gm/min)	REST	5'	30'	END EX
RT. KIDNEY	4.60 ±1.29(7)	2.54 0.70(7)	3.63 1.09(7)	2.68 0.56(7)
LT. KIDNEY	4.45 ±1.33(7)	2.47 0.67(7)[c]	3.52 0.97(7)	2.60 0.69(7)
ADRENAL	1.51 ±0.65(6)	1.44 0.40(6)	2.81 0.58(6)	2.14 0.71(6)
RT. BRAIN	0.80 ±0.13(5)	0.70 0.22(5)	0.71 0.15(5)	0.61 0.06(5)
LT. BRAIN	0.82 ±0.11(5)	0.72 0.19(5)	0.73 0.18(5)	0.60 0.06(5)
RT. LUNG	0.46 ±0.36(7)	0.66 0.90(7)	1.73 1.08(7)	1.36 1.17(7)
LT. LUNG	0.40 ±0.30(7)	0.67 0.78(6)	1.62 0.95(7)	1.23 1.19(7)
STOMACH proximal	0.28 ±0.16(7)	0.14 0.06(7)	0.19 0.09(7)[b]	0.15 0.09(7)
STOMACH distal	1.13 ±0.79(7)[b]	0.47 0.26(7)[b]	0.43 0.31(7)	0.21 0.18(7)
DUODEUM	1.19 ±0.36(7)	0.40 0.15(7)	0.56 0.25(7)	0.45 0.16(7)
JEJUNUM proximal	1.24 ±0.44(7)[b]	0.55 0.25(7)[c]	0.48 0.22(7)	0.39 0.21(7)
JEJUNUM distal	0.92 ±0.54(7)[c]	0.37 0.11(7)	0.47 0.17(7)	0.35 0.14(7)[c]
ILEUM proximal	0.87 ±0.49(7)	0.35 0.13(7)	0.37 0.14(7)	0.23 0.14(7)
ILEUM distal	0.60 ±0.45(7)	0.27 0.12(7)	0.34 0.10(7)	0.23 0.13(7)
COLON proximal	0.45 ±0.11(7)	0.29 0.09(7)	0.34 0.11(7)	0.22 0.07(7)
COLON distal	0.38 ±0.11(7)	0.19 0.05(7)	0.34 0.19(7)	0.14 0.07(7)
SPLEEN	2.08 ±0.83(7)	0.37 0.43(6)	0.52 0.50(7)	0.24 0.23(6)
PANCREAS	1.69 ±0.35(7)	0.34 0.17(7)	0.93 0.27(7)	0.37 0.14(7)
LIVER	0.07 ±0.07(7)	0.11 0.10(7)	0.14 0.12(7)	0.11 0.11(7)

Values presented as Mean ±SD(N)

[a] = p<.01, [b] = p<.05, [c] = p<.1 compared to fasting.

Table 21b. Post-Feeding Organ Blood Flows of Control Trained pigs during 2-hour runs at 65% of Heart Rate Reserve

ORGAN (ml/gm/min)	REST	5'	30'	END EX
HEART:				
RV-epi	0.96 +0.11(5)	2.76 0.66(5)	2.47 0.62(5)	3.16 0.86(5)
RV-endo	1.20 ±0.17(5)	3.09 0.78(5)	2.76 0.62(5)	3.56 1.04(5)
LV-epi	1.25 +0.26(5)[c]	2.29 0.54(5)	2.25 0.43(5)	2.90 0.89(5)
LV-endo	1.43 +0.15(5)	2.70 0.87(5)	2.52 0.66(5)	3.19 1.01(5)
LV-mid	1.53 ±0.35(5)	2.72 0.94(5)	2.62 0.69(5)	3.34 1.15(5)
SEPTUM-epi	1.20 +0.28(5)	2.86 0.79(5)	2.66 0.66(5)	3.30 0.89(5)
SEPTUM-endo	1.22 +0.19(5)	2.82 0.85(5)	2.73 0.59(5)	3.31 0.98(5)
SEPTUM-mid	1.43 ±0.26(5)	2.97 0.82(5)	2.86 0.62(5)	3.47 0.97(5)
SKELETAL MUSCLES:				
R Diaphragm	0.24 +0.05(5)	0.69 0.10(5)[a]	0.52 0.13(5)	0.63 0.22(5)
L Diaphragm	0.20 0.07(5)	0.68 0.13(5)[c]	0.48 0.16(5)	0.72 0.27(5)
Trapezius	0.15 +0.10(5)	0.75 0.27(5)	0.73 0.22(5)	0.76 0.24(5)
R Tricepts Lng Hd	0.12 +0.09(4)	0.80 0.25(5)	0.78 0.32(5)	0.81 0.29(5)
R Brachialis	0.13 +0.14(4)	1.88 0.20(5)	1.86 0.23(5)	1.88 0.21(5)
R Soleus	0.30 +0.14(7)[b]	0.35 0.11(7)	0.59 0.30(7)	0.56 0.16(7)
R Biceps Fem	0.17 +0.10(7)	0.80 0.31(7)	0.99 0.20(7)	0.91 0.18(7)[c]
R Semitendinosis	0.09 +0.08(7)	0.44 0.26(7)	0.44 0.21(7)	0.40 0.25(7)
R Rectus Femoris	0.05 +0.04(7)	0.80 0.47(7)	0.80 0.47(7)	0.76 0.34(7)
R Tibialis Ant	0.08 +0.08(6)	1.12 0.47(7)	1.15 0.31(7)	0.94 0.37(7)[c]
R Intercostal	0.11 +0.07(5)	0.45 0.37(5)	0.48 0.[illegible](5)	0.56 0.55(5)
R Lats	0.04 +0.03(4)	0.30 0.11(5)	0.26 0.10(5)	0.32 0.08(5)
Ventral Neck	0.06 +0.04(4)	0.28 0.15(5)	0.24 0.17(5)	0.32 0.21(5)[c]
Cremaster	0.06 ±0.03(7)	0.24 0.24(7)	0.22 0.15(7)	0.31 0.22(7)

Values presented as Mean ± SD(N)

[a] = p<.01, [b] = p<.05, [c] = p<.1 compared to fasting.

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b RESTRICTIVE MARKINGS None
2a. SECURITY CLASSIFICATION AUTHORITY N/A	3 DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release; distribution unlimited.
2b DECLASSIFICATION / DOWNGRADING SCHEDULE N/A	
4. PERFORMING ORGANIZATION REPORT NUMBER(S) NHRC Report No. 88-3	5 MONITORING ORGANIZATION REPORT NUMBER(S)
6a NAME OF PERFORMING ORGANIZATION Naval Health Research Center 6b OFFICE SYMBOL (If applicable) 70	7a. NAME OF MONITORING ORGANIZATION Commander, Naval Medical Command
6c. ADDRESS (City, State, and ZIP Code) P.O. Box 85122 San Diego, CA 92138-9174	7b. ADDRESS (City, State, and ZIP Code) Department of the Navy Washington, DC 20372
8a. NAME OF FUNDING / SPONSORING ORGANIZATION Naval Medical Research & Development Command 8b OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code) Naval Medical Command National Capital Region Bethesda, MD 29814-5044	10 SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. 63763A PROJECT NO. 3M26376 30819 TASK NO .AD.141 WORK UNIT ACCESSION NO. DA307899

11. TITLE (Include Security Classification) (U) THE EFFECTS OF ADAPTATION TO A LOW CARBOHYDRATE/HIGH FAT DIET AND PRE-EXERCISE FEEDING ON EXERCISE ENDURANCE, METABOLSIM, AND CARDIOVASCULAR DYNAMICS IN SWINE

12. PERSONAL AUTHOR(S) Gray, C.G., McKirnan, M.D., White, F.C., Mandarino, L., Sun, G., Niles, J.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15 PAGE COUNT
Interim	FROM 12/84 TO 12/87	1988 Jan	53

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Exercise, Diet, Metabolism, Endurance, Cardiovascular, Organ Blood Flow

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

A series of studies were performed on six groups of sedentary or moderate intensity exercise (MODX) miniature swine to evaluate the effects of: 1) adaptation to a low carbohydrate(7%)/high fat(74%) diet (A-LCD) on MODX endurance and metabolism; and 2) preexercise feeding on MODX endurance, metabolism, and blood flow distribution to muscles and organs. MODX was performed for up to five hours during the exercise studies. A-LCD resulted in a 30% increase in endurance; lower utilization of carbohydrate for energy, as evidenced by higher blood glucose and lower lactate; lower blood triglyceride and cholesterol; and decreased insulin sensitivity. Pre-exercise feeding resulted in greater cardiac output and oxygen consumption; reduced myocardial blood flow(BF); reduced active muscle BF; and increased gastrointestinal BF. Other results and implications are discussed.

20 DISTRIBUTION / AVAILABILITY OF ABSTRACT ☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT ☐ DTIC USERS	21 ABSTRACT SECURITY CLASSIFICATION Unclassified
22a NAME OF RESPONSIBLE INDIVIDUAL CDR C. G. GRAY, MC, USN	22b TELEPHONE (Include Area Code) (619)553-8453 22c OFFICE SYMBOL 70

DD FORM 1473, 84 MAR 83 APR edition may be used until exhausted
All other editions are obsolete

SECURITY CLASSIFICATION OF THIS PAGE

GPO: 1988—607-047